Midterm Results of the Treatment of Cartilage Defects in the Knee Using Alginate Beads Containing Human Mature Allogenic Chondrocytes

Aad A.M. Dhollander,*†‡ MD, Peter C.M. Verdonk,†§ MD, PhD, Stijn Lambrecht,‡ PhD, René Verdonk,† MD, PhD, Dirk Elewaut,‡ MD, PhD, Gust Verbruggen,‡ MD, PhD, and Karl Fredrik Almqvist,† MD, PhD
Investigation performed at Ghent University Hospital, Ghent, Belgium

Background: The treatment of chondral lesions is still an important challenge for the orthopaedic surgeon. Attempts have been made to restore cartilage lesions by filling the defects with a temporary biocompatible matrix.

Purpose: The authors present their midterm experience with the implantation of alginate beads containing human mature allogenic chondrocytes for the treatment of cartilage lesions in the knee.

Study Design: Case series; Level of evidence, 4.

Methods: A biodegradable, alginate-based biocompatible scaffold containing human mature allogenic chondrocytes was used for the treatment of cartilage lesions in the knee. Twenty-one patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a visual analog scale (VAS). The mean follow-up time was 6.3 years (range, 5-8 years). Magnetic resonance imaging (MRI) data were analyzed based on the MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) system, allowing morphologic assessment of the repair tissue. Magnetic resonance images were taken at 1 year of follow-up and at a mean follow-up of 6.1 years (range, 5-7 years).

Results: During the follow-up period, the WOMAC and VAS scores improved significantly. No signs of clinical deterioration or adverse reactions to the alginate beads/allogenic chondrocyte implantation were observed. Four failures occurred during the follow-up period in this study (19.05%). The MOCART scores were moderate and remained stable in time.

Conclusion: This investigation provided useful information on the efficacy of the implantation of alginate beads containing human mature allogenic chondrocytes for the treatment of cartilage lesions in the knee. The midterm clinical outcome of the presented technique was satisfactory. However, these results were not confirmed by the MRI findings.

Keywords: allogenic; chondrocyte; alginate; cartilage; knee; implant

Articular cartilage lesions have become of major interest to orthopaedic surgeons because most lesions do not heal spontaneously.16 This poor repair capacity of cartilage has led to the development of various surgical techniques. The effectiveness of microfracture has been evaluated in human subjects.31 Patients treated with this technique often experience short-term pain relief and develop progressive symptoms because of repair tissue failure.15,25 It is now over 20 years since the first patient was operated on with autologous chondrocyte implantation (ACI).6 This technique has gained wide scientific and clinical support for use in the repair of focal articular lesions.29 However, during in vitro propagation of the chondrocytes, dedifferentiation of the cells can occur, and afterward these fibroblast-like chondrocytes show different biosynthetic properties than the original cartilage cells in the knee joint.4

In this way, characterized chondrocyte implantation (CCI) has been developed to improve the results of articular regeneration with chondrocyte cell therapy through the use of a cell population capable of making stable hyaline-like cartilage in vivo.30 Characterized chondrocytes are an expanded population of chondrocytes that expresses a marker profile (a gene score) predictive of the capacity to form hyaline-like cartilage in vivo in a consistent and reproducible manner.3
Another way to avoid the issue of dedifferentiation during in vitro propagation of chondrocytes could be the use of instantaneously delivered allogenic chondrocytes. Previous research has shown that human chondrocytes keep their phenotype in alginate with neosynthesis of an extracellular matrix and that this chondrocyte/alginate culture setup can be biologically frozen without any impairment in the total of overall aggrecan synthesis rates or its cartilage-specific aggrecan subtypes once thawed. Ideally, this could lead to the construction of a chondrocyte donor bank with cell batches ready for use in large numbers of patients.

A pilot study was started to evaluate the use of a biodegradable, alginate-based biocompatible scaffold containing human allogenic chondrocytes for the treatment of cartilage lesions in the knee. This technique was developed in 2002 and the procedure has been performed in 21 patients. The short-term results of this pilot study showed that the proposed procedure was feasible and safe for the treatment of symptomatic cartilage defects of the knee. The described technique provided clinical and histologic outcomes that were equal to those of other cartilage repair techniques. However, the promising short-term clinical outcome of the allogenic chondrocytes/alginate beads implantation was not confirmed by the short-term MRI findings. The goals of this study were to assess whether the clinical improvements observed in the pilot study at 2 years continued at midterm follow-up and to reevaluate the initial moderate MRI findings at midterm follow-up.

MATERIALS AND METHODS

Study Population

Patients with focal cartilage defects involving the femoral condyles, patellas, and trochlea, and with clinical symptoms (pain, swelling, locking, and “giving away”) were eligible for treatment. Exclusion criteria were an age under 10 and above 60 years, untreated tibiofemoral or patellofemoral malalignment or instability, diffuse osteoarthritis or bipolar “kissing” lesions, major meniscal deficiency, and other general medical conditions such as diabetes or rheumatoid arthritis. Clinical experimentation was approved by the Hospital Ethics Committee and informed consent to participate in the study and to comply with the postoperative regimen was obtained from all patients.

Twenty-one patients (13 males, 8 females) were treated consecutively since October 2002 as published previously. The mean follow-up time was 6.3 years (range, 5-8 years). Briefly, the right/left (R/L) ratio was 12/9. In all these cases, the lesions were focal. Fifteen chondral defects were located on the medial femoral condyle (MFC), 4 on the lateral femoral condyle (LFC), 1 on the patella, and 1 on the trochlea. All lesions were ICRS (International Cartilage Repair Society) grade III or IV and had a mean size of 2.6 cm² (range, 1.9-26 cm²). The origin was traumatic in 12 cases and focal degenerative in 9 cases. The mean age of the patients was 33 years (range, 12-47 years). The mean duration of symptoms prior to surgery was 33.20 months (range, 6-73 months).

Previous surgery in 10 of the patients (47.62%) included 6 partial meniscectomies, 2 anterior cruciate ligament (ACL) reconstructions, 1 meniscal suture, and 5 cartilage repair operations, such as shaving (1), debridement (2), and microfracturing (2) of chondral lesions. In 5 patients, associated procedures were performed: 1 ACL reconstruction, 1 Fulkerson osteotomy, 1 high tibial osteotomy, and 1 lateral and 1 medial allogenic meniscal transplantation. Detailed individual patient characteristics were published previously.

At the beginning of this study, the patient cohort consisted of 21 individuals. The patients were followed prospectively and evaluated yearly. At 3 years of follow-up, 2 of the 21 patients (9.52%) were lost to follow-up, another 2 (9.52%) at 4 years of follow-up when they changed their addresses. Clinical data of 18 patients were available at 3 years of follow-up, of 15 patients at 4 years, of 14 patients at 5 years, of 9 patients at 6 years, of 7 patients at 7 years, and 1 patient achieved 8 years of follow-up.

Chondrocyte Harvesting and Culture

Human articular chondrocytes were isolated as described before. All allogenic cartilage cells used were obtained from the Ghent Tissue Retrieval Programme following the restrictions imposed by the European/Belgian requests for tissue banks. Human articular cartilage was obtained from the femoral condyles of different donors within 24 hours of death. All donors had died after a short illness and were under 40 years of age. None of them had received corticosteroids or cytostatic drugs. Visually intact cartilage was harvested from the femoral condyles and diced into small fragments. The chondrocytes were isolated by sequential enzymatic digestion of the extracellular matrix. Chondrocyte cultures in alginate beads were then prepared as described previously. The chondrocytes in the alginate beads were cultured for 2 weeks in a 6-well plate in an incubator at 37°C under 5% CO₂. Three milliliters of Dulbecco’s modified Eagle medium (DMEM, Gibco BRL, Grand Island, New York) supplemented with 10% acceptor serum and 50 μg freshly dissolved ascorbate per milliliter were then added and replaced 3 times weekly.

Surgical Technique

A miniarthrotomy was performed to properly reach the defect. After the carefully performed debridement of the defect back to stable walls of healthy cartilage, the lesion was measured. Once the defect was cleaned and ready to accept the alginate beads, it was sealed with a peristeal flap with the cambium layer facing the defect. Before the defect was sealed completely, a small opening was left unsutured for implantation of the alginate beads. The alginate beads were inserted manually. Subsequently, the open edge of the flap was sutured to the remaining borders of the defect (Figure 1), which was then easily sealed watertight with fibrin glue (Baxter, Deerfield, Illinois). The periosteal flap was sutured with single resorbable Vicryl 6/0 stitches (Ethicon, Somerville, New Jersey). The periosteal flap was harvested from the proximal tibia. The postoperative regimen consisted of non-weightbearing
Achieving a normal gait pattern was advised at 10 weeks postoperatively. Maximum active flexion did not exceed 90° for the first 4 weeks of rehabilitation. Full range of motion was allowed 8 weeks postoperatively. Isometric quadriceps training, straight-leg raising, and hamstrings isometrics were advised after the first 2 weeks. Return to low-impact sports was allowed 12 months after surgery. All patients were compliant to these guidelines.

Clinical Evaluation
All 21 patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a visual analog scale (VAS) for pain preoperatively and yearly after the procedure. The WOMAC is a valid, reliable, and sensitive instrument for the detection of clinically important changes in health status. It has already been used for the clinical evaluation of cartilage repair techniques in different studies. The VAS for pain is a simple, reliable, and valid measurement instrument that measures the amount of pain a patient feels, ranging across a continuum from none to extremely severe.

Magnetic Resonance Imaging Technique
All MRI examinations were performed on a 1.5-T or a 3-T MRI unit (either a MAGNETOM Avanto, a MAGNETOM Symphony Tim, or MAGNETOM Trio, Siemens Medical Solutions, Erlangen, Germany). Of the 21 patients, 12 (57%) had consented to undergo MRI evaluation protocol at 1 year of follow-up and 9 of these 12 patients (76%) at a mean follow-up of 6.1 years (range, 5-7 years). We performed a standard knee MRI protocol including proton-density and T2-weighted turbo spin echo (TSE) acquisitions using a dedicated send-receive 8-channel knee coil. As previously published, imaging parameters of the sequences were as follows: (1) sagittal proton density and T2-weighted TSE images (TE, 24/96 milliseconds; repetition time [TR], 4000 milliseconds on 1.5 T; TE, 29/101 milliseconds; TR, 4662 milliseconds on 3 T; slice thickness, 3 mm with a 0.3-mm intersection gap; field of view [FOV], 180 mm; matrix size, 512 × 307 on 1.5-T MRI unit, 448 × 246 on 3-T unit), (2) coronal proton-density-weighted images with fat saturation (TE, 43 milliseconds; TR, 4400 milliseconds on 1.5 T; TE, 44 milliseconds; TR, 3140 milliseconds on 3 T; slice thickness, 3 mm; FOV, 180 mm; matrix size, 512 × 240 on 1.5-T MRI unit, 448 × 218 on 3-T unit), (3) transverse 3-dimensional (3D) dual-echo steady-state (DESS 3D) images, a gradient echo (GRE) sequence (TE, 5.6 milliseconds; TR, 19 milliseconds; flip angle, 25°; slice thickness, 3 mm; FOV, 160 mm; matrix size, 256 × 156), (4) sagittal 3D fast low-angle shot images with water excitation images (FLASH 3Dwe) (only on 1.5-T MRI unit), spoiled GRE (TE, 27.0 milliseconds; TR, 13.7 milliseconds; flip angle, 30°; slice thickness, 1 mm consecutively; FOV, 180 mm; matrix size, 512 × 240), and (5) sagittal 3D proton-density SPACE (sampling perfection with application-optimized contrasts using different flip-angle evolution) images with fat saturation (only on 3-T MRI unit) (TE, 43 milliseconds; TR, 1100 milliseconds; slice thickness, 0.6 mm; FOV, 160 mm; matrix size, 320 × 269) (Figure 2).

Original and Modified MOCART System
For the description of the repair tissue, we used the original MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) system previously published by Marlovits et al. Nine variables were used to describe the morphologic characteristics and signal intensity of the repair tissue compared with the adjacent native cartilage. Besides the original MOCART system, we also used a modification of this system previously published by Dholander et al. Both morphologic MRI classification systems were applied to the magnetic resonance images.
Mean values and standard deviations of the visual analog scale (VAS) for pain: preoperative (pre) (n = 21; 89.40 ± 35.51) and postoperative: 1 year (n = 20; 8.65 ± 12.95; 0–1 year, P = .001), 2 years (n = 20; 15.65 ± 17.84; 0–2 years, P = .001), 3 years (n = 18; 17.06 ± 14.71; 0–3 years, P = .001), 4 years (n = 15; 13.33 ± 12.81; 0–4 years, P = .001), 5 years (n = 14; 12.79 ± 11.18; 0–5 years, P = .001), 6 years (n = 9; 6.67 ± 7.50; 0–6 years, P = .008), 7 years (n = 7; 15.43 ± 26.73; 0–7 years, P = .028), and 8 years (n = 1; 9.00). Values are expressed in millimeters. The black dots indicate statistically significant differences (P < .05) between the preoperative and postoperative values.

Figure 3. Mean values and standard deviations of the visual analog scale (VAS) for pain: preoperative (pre) (n = 21; 89.40 ± 35.51) and postoperative: 1 year (n = 20; 8.65 ± 12.95; 0–1 year, P = .001), 2 years (n = 20; 15.65 ± 17.84; 0–2 years, P = .001), 3 years (n = 18; 17.06 ± 14.71; 0–3 years, P = .001), 4 years (n = 15; 13.33 ± 12.81; 0–4 years, P = .001), 5 years (n = 14; 12.79 ± 11.18; 0–5 years, P = .001), 6 years (n = 9; 6.67 ± 7.50; 0–6 years, P = .008), 7 years (n = 7; 15.43 ± 26.73; 0–7 years, P = .028), and 8 years (n = 1; 9.00). The black dots indicate statistically significant differences (P < .05) between the preoperative and postoperative values.

taken at 1 year of follow-up and at a mean follow-up of 6.1 years (range, 5–7 years). All magnetic resonance images were evaluated by an independent reviewer. Both the original and modified MOCART scores were expressed as a percentage of the maximum score.\textsuperscript{9,10}

Statistical Methods

All data are expressed in terms of means and standard deviations. The Wilcoxon test was used to analyse statistical differences between the preoperative and follow-up WOMAC and VAS pain scores, between the postoperative values of the original MOCART system, and between the postoperative values of the modified MOCART system. For all tests, P < .05 was considered significant. Statistical analysis was performed using PASW statistics 18 (SPSS Inc, Chicago, Illinois).

RESULTS

Clinical Outcome

During the follow-up period, the VAS scores for pain indicated by the patients improved significantly (Figure 3). The differences between the preoperative and postoperative values were statistically significant (P < .05). The postoperative VAS scores for pain remained quite stable over time.

All mean total WOMAC scores decreased when preoperative and postoperative values were compared (Figure 4). The differences between the preoperative score and the scores obtained at all study points after the allogenic chondrocyte implantation were statistically significant (P < .05).

All WOMAC subscale scores (physical function, pain, and stiffness) improved when preoperative and postoperative values were compared (Figure 5). The WOMAC scores for physical function and for pain were statistically significantly ameliorated at all follow-up periods (P < .05). The WOMAC scores for joint stiffness were significantly improved until 6 years of follow-up (P < .05). The improvement in joint stiffness was not statistically significant anymore at 7 years of follow-up (P > .05).

Four failures were observed among the 21 patients until now (19.05%). One early failure occurred because of loosening of the periosteal flap, which was attributed to a failure of the surgical procedure.\textsuperscript{1,10} Another 3 failures were observed—one at 3 years, 1 at 5 years, and 1 at 6 years postoperatively. A delamination of the repair tissue because of trauma was observed in the first case. A progressive deterioration of the clinical status was observed in the latter 2 patients. Magnetic resonance imaging data were available of the last failure showing a thinning of the repair tissue and the formation of several subchondral cysts. These 2 patients elected to undergo joint arthroplasty. No correlation could be found between the failures and size of the lesion.

Figure 4. Mean values and standard deviations of the total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores: preoperative (pre) (n = 21) (46.40 ± 25.86) and postoperative: 1 year (n = 20; 6.25 ± 8.64; 0–1 year, P = .001), 2 years (n = 20; 14.42 ± 20.04; 0–2 years, P = .001), 3 years (n = 18; 15.28 ± 15.19; 0–3 years, P = .001), 4 years (n = 15; 13.86 ± 13.86; 0–4 years, P = .001), 5 years (n = 14; 13.86 ± 13.86; 0–5 years, P = .001), 6 years (n = 9; 8.56 ± 9.08; 0–6 years, P = .008), 7 years (n = 7; 12.14 ± 14.48; 0–7 years, P = .018), and 8 years (n = 1; 8.00). The black dots indicate statistically significant differences (P < .05) between the preoperative and postoperative values.
As with the original MOCART system, a higher modified MOCART system score signified a more cartilage-like aspect of the repair tissue on MRI. The modified MOCART percentages also decreased over time (—12.46%) (Figure 6B). The differences between 1-year and midterm follow-up were not statistically significant (P = .262), as seen with the original MOCART scores. Both MOCART scoring methods indicated that the condition of the repair tissue deteriorated on MRI.

### MRI Data Evaluated With the Original MOCART System at 1-Year and Midterm Follow-up

At 1-year and at midterm follow-up after the allogenic chondrocyte implantation, the MRI data were analyzed according to the original MOCART system (see Appendix 1, available in the online version of this article at http://ajs.sagepub.com/supplemental). Complete filling of the defect was found in 1 case (8.3%) at 1 year and in 2 cases (22.2%) at midterm. Hypertrophy of the repair tissue was seen in 4 cases (28.6%) at 1 year. Only 1 case of hypertrophy was observed at the midterm follow-up period (11.1%). Twelve months after the procedure, a complete integration of the border zone with the adjacent cartilage was detected in 5 patients (41.7%). This finding was seen only once, at a mean follow-up of 72 months (11.1%). The surface of the repair tissue was intact in 2 patients (16.7%) and had a homogeneous structure also in 2 (18.7%) patients at 1-year follow-up. The midterm MRI evaluation of the repair tissue showed a damaged surface of the repair tissue in all cases and a homogeneous structure in only 1 case (11.1%). Adhesions were present in 1 patient at 1-year follow-up (16.7%), but not observed later on. Four patients (25%) showed an effusion 1 year after the procedure and 6 patients at the midterm evaluation point (67%). Concerning the signal intensities of the repair tissue, the numbers of markedly hypointense or hyperintense observations increased over time. The subchondral lamina was damaged in all cases at both observation periods. Finally, an intact subchondral bone was seen in 7 patients (58.3%) 1 year after the operation. However, the midterm MRI findings showed in all cases subchondral bone changes. Moreover, the formation of intralesional osteophytes was observed in 4 patients (44.5%) (Figure 7).

### DISCUSSION

The treatment of chondral lesions is still an important challenge for the orthopaedic surgeon because of the difficulty in restoring the damaged areas with hyaline cartilage. Several techniques have been used in the operative treatment of cartilage lesions: marrow stimulation techniques, osteochondral graft transplantation, ACI, and new procedures based on acellular scaffolds. In the present study, alginate beads containing human allogenic chondrocytes were used for the treatment of cartilage defects in the knee. This procedure is a novel cellular-based technique that obviates the need for harvesting and culturing autologous chondrocytes and is performed in a single-step procedure. The patients who participated in this study showed a strong clinical improvement.

### Longitudinal Evaluation of the Repair Tissue With the Original and Modified MOCART System

Magnetic resonance imaging evaluation of the repair tissue was performed at 1 year of follow-up and at a mean follow-up of 6.1 years (range, 5-7 years). The original MOCART scores decreased over time (—13.68%) (Figure 6A). However, there were no statistically significant differences between 12-month and midterm follow-up (P = .23). As with the original MOCART system, a higher modified MOCART system score signified a more cartilage-like aspect of the repair tissue on MRI. The modified MOCART percentages also decreased over time (—12.46%) (Figure 6B). The differences between 1-year and midterm follow-up were not statistically significant (P = .262), as seen with the original MOCART scores. Both MOCART scoring methods indicated that the condition of the repair tissue deteriorated on MRI.

![Physical function, Pain, Stiffness](image-url)
after surgery, as shown by the significantly improved WOMAC and VAS pain scores (Figures 3 through 5). This improvement remained quite stable over time. No signs of clinical deterioration were observed during the midterm evaluation period. Most of the cartilage repair techniques report favorable clinical outcomes at different follow-up times.18,20,27,31 As described in the Results, 4 failures were observed during the follow-up period in this study (19.05%) and 4 patients were lost to follow-up (19.05%). Peterson et al18 reported a failure rate of 6.93% in their midterm results of ACI. Minas et al24 published a failure rate of ACI between 8% and 26% depending on whether the patients were treated previously with microfracture or not. The 19.05% failure rate observed in this study is quite high compared with those published by others. However, one must take into account the high number of previous and associated surgeries performed in these patients, making them a challenging patient cohort.

In the literature, most of the studies report the clinical outcome at different follow-up times. However, a systematic evaluation of the repair tissue has only been done in a few studies.18,20 The gold-standard method for the imaging evaluation of cartilage lesions is MRI.18,28 We opted for the MOCART system because it was found to be a valid, accurate, and reproducible MRI grading and scoring method.31 In the present study, both the original and modified MOCART systems were used in a longitudinal fashion to evaluate the repair tissue (Figure 6). The scores were presented as a percentage of the maximum scores, as published before.9,10 In this way, a comparison between both MOCART systems was possible. The modified MOCART system was developed by giving more weight to certain variables in an attempt to increase the prognostic value of the scoring system and should be considered as an incentive for further research to develop a true prognostic and valid MRI scoring system.10 Both original and modified MOCART scores were moderate and remained stable over time. Remarkably, the modified MOCART scores were lower compared with the original MOCART scores. This is probably because of the increased weight given to the subchondral lamina and bone changes.

Based on the original MOCART system published by Marlovits et al,21 we analyzed the MRI data at 1 year postoperatively and at a mean follow-up of 6.1 years (see Appendix 1, available online). At midterm, we observed a complete filling of the defect or hypertrophy in 33.3% of the cases. Kon et al18 reported, in their series of patients treated with second-generation ACI, a complete filling of the defect in 66.0% at a minimum follow-up of 5 years.
Remarkably, the subchondral lamina was not intact in any of the cases treated with the allogenic chondrocyte technique presented in this study and this was observed at both follow-up times. Moreover, the aspect of the subchondral bone worsened over time. This is a quite troublesome finding compared with the results published by Kon et al concerning the second-generation ACI. They observed an intact subchondral lamina in 46.0% and an intact subchondral bone in 60.0% of the cases. The number of patients with effusion increased over time from 25.0% to 66.7% in the presented patient cohort. At 5 years of follow-up, patients treated with second-generation ACI showed effusion in only 37.5% of the patients. Taken all together, the results of the evaluation of the MRI data with the original MOCART system concerning the allogenic chondrocyte implantation are inferior to those published by Kon et al concerning second-generation ACI.18

In general, in this study there is a remarkable difference between the favorable clinical outcome and the moderate to poor MRI findings. Clinical scores give a subjective momentary image of the patient's status and cannot predict the long-term durability of the good outcome.27,28 A possible explanation for the discrepancy between the clinical outcome and MRI findings could be that patients treated for a cartilage lesion adapt their expectations in time and are more satisfied with less knee function as time passes. However, the true natural history of cartilage defects remains unclear. Mandelbaum et al noted that well-contained, isolated defects smaller than 2 cm may be asymptomatic and nondegenerative. This might also be an explanation for the discrepancy between imaging and clinical outcome. It is clear that only further longer follow-ups and larger high-level MRI studies can solve this issue.

Tissue-engineered cartilage by chondrocytes cultured in alginate has been reported by several authors.1,11,26 These studies confirmed the biocompatibility of alginate as a temporary carrier. In this study, as expected in a nonvascularized tissue such as cartilage, no serious adverse reactions to the alginate matrix seeded with allogenic chondrocytes were observed. We have chosen alginate as a scaffold for cell seeding because of its ability to stabilize the chondrocytic phenotype. Alginate enabled us to deliver the cells easily and homogeneously without the risk of leakage. The use of allogenic chondrocytes obviates the need for harvesting and culturing autologous chondrocytes. In this way, the problem of dedifferentiation during in vitro propagation of autologous chondrocytes was avoided. It was calculated from our donor data that approximately 10 to 20 patients could theoretically benefit from a single donor. In the future, this technique could be optimized by using a synthetic membrane instead of the peristomal flap; by selecting the donors on certain ideal characteristics such as age, donor site, and physical condition; and by enhancing the chondrogenic capacity of the alginate matrix by changing its chemical structure and characteristics or by adding growth factors.1

Finally, the surgical procedure presented in this study is a novel technique. The midterm clinical outcome is satisfactory. No signs of severe clinical deterioration were observed. However, the clinical outcome was not confirmed by the MRI findings. In general, the MRI data were moderate and remained stable in time. The weaknesses of this study were the nonrandom selection of the patient population, the lack of a control group, and the limited number of patients treated. However, this investigation provided useful information on the efficacy of this new treatment in chondral lesions of the knee and inspires us to search for further improvements of this technique. These improvements are mandatory to allow the setup of large-scale, long-term, randomized controlled trials to confirm the reliability of this procedure.

ACKNOWLEDGMENT

The authors thank K. Verstraete and W. Huyse of the Department of Radiology at Ghent University for their support concerning the application of the MRI facilities.

REFERENCES


